

REMARKS

Reconsideration of this application is respectfully requested.

Claims 454-575 are pending in this application. No claim has been amended or deleted. No new claims have been added. Accordingly, the claims 454-575 are presented for further examination on the merits.

The First Rejection Under 35 U.S.C. §112, First Paragraph

Claims 459-472 and 474-575 stand rejected under 35 U.S.C. §112, first paragraph. In the Office Action (pages 2-3) the Examiner stated that these claims contain:

"subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons of record. This is a "new matter" rejection.

Support was not found where indicated in the specification, nor elsewhere, for the following limitations in Claims 459-472 and 474-575:

Claims 459-463, specific chemical compositions of linkages;

Claims 464-472, 482-569, specific identity of labels and points of attachment of the "SIG" moiety to internal phosphates;

Claims 474-477 and 570-575, the "composition" limitation, in addition to the above identified limitations.

Applicant argues in the response, pages 30-32, that support was found in various portions of the specification. This argument is not persuasive. These portions merely recite support for covalent attachment of a SIG moiety to a phosphate moiety and a SIG moiety to the oxygen on a phosphate moiety. Note, there is no support for the attachment of the SIG moiety to the phosphate atom of the phosphate moiety, only to the oxygen atom."

This rejection is respectfully traversed. Example V on page 57 of the specification does in fact disclose Sig attached directly to the phosphorous atom of the phosphate moiety (PM). Additionally an enlarged copy of the Halloran Figure 1, including reaction 2, does reveal that Halloran depicts the Phosphate moiety ENZ-5(D6)(C2)

attachment to a phosphate atom. Examiner acknowledges the Halloran disclosure at pages 3 and 4, and one only needs to glance at the Halloran reference to see the attachment points to understand the invention being disclosed and conveyed by this application.

In view of the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of this rejection under 35 USC 112.

The Second Rejection Under 35 U.S.C. §112, First Paragraph

Claims 454-575 stand rejected for enablement under 35 U.S.C. 112, first paragraph, as "containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record." (Office Action, page 3).

The Examiner states on pages 3-4 of the Office Action that:

Applicant argues that the prior art, such as Halloran, supports enablement. This argument is not persuasive for several reasons:

Halloran discloses the attachment of a specific signal moiety, a protein, to the phosphorus atom of the phosphate moiety using a specific linker, a $-C-(CH_2)_4-N-$ chain. In contrast, the claims are drawn to a much broader category, a generic "SIG" moiety and linkage, and specific compounds such as those recited in claim 464 -- magnetic, hormone, metal containing "SIG" moieties, for example. Thus, the scope of the enablement is not commensurate with the scope of the claims.

In addition, several of the reference articles are drawn to labeling a mononucleotide and express doubt about labeling an oligonucleotide. Armstrong et al., Eur. J. Biochem. 0:33-38, 1976, teaches that the labeled mononucleotides are "strong competitive inhibitors" of the reaction which is necessary to produce a labeled oligonucleotide from a labeled mononucleotide. See Armstrong, p. 33, col. 1. This reaction is the use of the labeled mononucleotide as a substrate for the polymerase mediated synthesis of the oligonucleotide.

While Armstrong teaches that some labeled mononucleotide will be incorporated, Armstrong teaches no guidance as to which of the myriad labels within the scope of these claims will function in the claimed invention. Lacking any guidance in the specification and in view of the breadth of the claims, it would require undue experimentation in order to enable a reasonable number of embodiments of these claims. The skilled artisan would have to

experiment with various SIG moieties, linkages and attachment sites, as well as various reaction protocols and protecting groups.

This enablement rejection is respectfully traversed. One skilled in the art and armed with the present disclosure would have sufficient guidance to practice the invention over the entire claimed range. Applicants are in the process of gathering expert testimony and articles to support their position and will submit such information in a supplemental response.

Applicants respectfully request reconsideration and withdrawal of the rejection for lack of enablement.

The First Rejection Under 35 U.S.C. §103

Claims 454-575 stand rejected under 35 U.S.C. § 103 for being unpatentable over Gohlke et al., US Patent 4,378,458, 3/1983, filed 3/1981 (Gohlke) in view of Sodja et al., Nucleic Acids Res., 5(2):385-401, 1978 (Sodja) and further in view of applicant's admissions.

On pages 4-5 of the Office Action, the Examiner stated that:

Applicant argues that the opening of the ring sugar in Sodja distinguishes Sodja from the e current application. It is argued that the terminal nucleotide, with the open sugar, is outside the scope of the claims.

This argument is not persuasive. Sodja reads on the claimed invention because of the scope of the term "SIG" moiety. There is nothing in the limitation "SIG" which would exclude the terminal nucleotide, with the open ribose sugar from being a part of the "SIG" moiety. The "terminal" nucleotide in the claimed product would be the second nucleotide from the end in the Sodja reference, which has a closed ribose sugar ring.

Applicant argues that Gohlke does not teach labeling ribonucleotides and thus does not suggest the claimed DNA products. This argument is not persuasive. First, many of the claims of this case are not limited to DNA products but read on ribonucleotides. Second, it is Gohlke in view of Sodja which is the basis of the rejection. There is no evidence that Gohlke cannot be applied to Sodja for the expected benefit of generating other types of labeled oligonucleotides using the Gohlke labels.

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This obviousness rejection is respectfully traversed. Applicants respectfully maintain that the differences between the instant invention and the combination of cited documents would not have been obvious to one of ordinary skill in the art at the time of the invention. Halloran was published 29 years before this application was deposited, Miller was published 14 years before; it was the applicants who first came to the realization of this invention. Thus, it would be unpermitted hindsight for one to use the current application to apply teachings from the prior art to "reinvent" the invention.

Reconsideration and withdrawal of the obviousness rejection is respectfully requested. Applicants are in the process of detailing additional arguments to support their position of non-obviousness over the cited references and will submit these arguments in a supplemental response shortly.

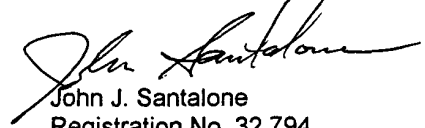
In view of the above amendments and foregoing remarks, Applicants respectfully request reconsideration and withdrawal of the anticipation rejection, thereby placing each of claims in allowable condition.

SUMMARY AND CONCLUSIONS

No other fees are believed due in connection with this filing. In the event that any other fee or fees are due, however, the Patent and Trademark Office is authorized to charge the amount of any such fee(s) to Deposit Account No. 05-1135, and to credit any overpayment thereto.

In view of the above discussion of the issues, Applicants respectfully submit that all of the instant claims are in allowable condition. Should it be deemed helpful or necessary, the Examiner is respectfully invited to telephone the undersigned at (212) 583-0100 to discuss the subject application.

Respectfully submitted,


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